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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,943	10/16/2003	Andrew McMichael	2907.1000-003	4585

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	**PAPER NUMBER**
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,943	MCMICHAEL ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006 and 09 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *8,9,11,13,17-26,29,30,34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10,12,14-16,27,28 and 31-33* is/are rejected.

7)☒ Claim(s) *31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/9/06*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed on 09 November 2006 and 26 December 2006. Claims 1-35 are pending. Claims 8, 9, 11, 13, 17-26, 29, 30, 34 and 35 are withdrawn as being drawn to nonelected species. Claims 1-7, 10, 12, 14-16, 27, 28 and 31-33 are examined.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 09 November 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The objection to specification is withdrawn in view of the Applicant's amendment.

The Examiner notes with appreciation that Applicants are willing to file a terminal disclaimer should allowable subject matter be indicated. The nonstatutory double patenting rejection of claims 1-6, 10, 14-16, 27 and 31-33 as being unpatentable over claims 1, 2, 5-7, 15-18, and 20 of U.S. Patent No. 6,663,871 will be withdrawn upon Applicants' submission of a compliant terminal disclaimer..

The provisional nonstatutory double patenting rejection of claims 1-3, 6, 7, 10, 12, 14 and 15 as being unpatentable over claims 1, 4, 5, 9, 11, 13 and 14 of copending Application No. 10/833,439, of claims 1-3, 6, 7, 10, 12, 14 and 15 as being unpatentable over claims 1, 4, 5, 9, 11 and 13-16 of copending Application No. 10/833,744, of claims

1-3, 5-7, 10, 12, 14 and 15 as being unpatentable over claims 1, 4, 5, 9, 11, and 13-15 of copending Application No. 10/833,745, and of claims 1, 6 and 27 as being unpatentable over claims 1-5 and 6-8 of copending Application No. 10/653,624 are held in abeyance until allowable subject matter is determined.

Response to Arguments - 35 U.S.C. §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 2, 6, 7, 10, 12 and 14 under 35 U.S.C. §102(b) as being anticipated by Hodge *et al.* (1997, April-May) is **withdrawn** in view of the Applicants' argument based on the Schneider Declaration, originally filed in the parent Application No. 09/454,204, now U.S. Patent No. 6,663,871, which states that the antigen taught by Hodge *et al.*, "purified human CEA" or whole CEA protein, generates CD4+ T cell response. Therefore, Hodge et al. do not teach generating CD8+ T cell immune response.

Response to Arguments - 35 U.S.C. §103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-4, 6, 7, 10, 12, and 14-16 under 35 U.S.C. §103(a) as being obvious over Hodge *et al.* (1997) in view of Stoute *et al.* (1997) is **withdrawn** for the same reason as set forth above.

The rejection of claims 1-3, 6, 10, 12, 14 and 15 under 35 U.S.C. §103(a) as being obvious over Pialoux *et al.* (1995) in view of Egan *et al.* (1995) is **maintained**.

The amended claims are directed to a method for generating a CD8+ T cell immune response in a mammal against at least one target antigen, comprising administering to said mammal at least one dose of each of the following:

(i) a priming composition comprising a source of one or more CD8+ T cell epitopes of the target antigen; and

(ii) a boosting composition comprising a source of one or more CD8+ T cell epitopes of the target antigen, including at least one CD8+ T cell epitope, which is the same as a CD8+ T cell epitope of the priming composition, wherein the source of CD8+ T cell epitopes is a non-replicating or replication-impaired recombinant virus vector in the mammal;

with the proviso that if the source of epitopes in (i) is a viral vector, the viral vector in (ii) is derived from a different virus, wherein the CD8+ T cell immune response against at least one target antigen is boosted in the mammal.

Examiner's rejection in the Action mailed on 05 July 2006 is as follows:

Pialoux *et al.* describes a prime-boost approach to generate CD8+ T cell response against HIV, by injecting health adults with recombinant canarypox vector expressing the HIV-1 gp160, from the MN isolate, in a formulation with an adjuvant. See abstract.

Pialoux *et al.* does not disclose non-replicating viral boosting vectors.

Egan *et al.* suggests administrating non-replicating canarypox vectors expressing HIV gp160 from the MN isolate. See abstract.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify vectors of Pialoux *et al.* to non-replicating viral vectors. One having ordinary skill in the art would have been motivated to do this to ensure the safety of the immunogenic vectors in humans, as per suggested by Egan *et al.*, who established a reasonable expectation of success by describing the administration of non-replicating ALVAC vector for the induction of CD8+ HIV-1-specific CTL in adult humans. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argue that neither reference teach or suggest a boosting composition that is a non-replicating or replication-impaired recombinant virus vector. The combination of Pialoux *et al.* and Egan *et al.* teach the priming and boosting regimen in the reverse order as compared to the claimed invention, i.e. priming with an ALVAC expressing an HIV glycoprotein and boosting with a recombinant HIV protein. However, it would be obvious to one skilled in the art to prime and boost a subject using a protein subunit and an ALVAC vector expressing the same epitope in either order with reasonable expectation of success, absent evidence to the contrary. Egan's disclosure that ALVAC-HIV elicits CTL response does not limit the disclosure to a specific order of priming and boosting regimen.

The rejection of claims 1-3, 5, 6, 10, 12, 14 and 15 under 35 U.S.C. §103(a) as being obvious over Pialoux *et al.* (1995) in view of Egan *et al.* (1995), and further in view of Walker *et al.* (1989) is **maintained**.

The instant invention is further limited to CD8+ T cell epitope comprising an amino acid sequence of SEQ ID NO:64.

Examiner's rejection in the Action mailed on 05 July 2006 is as follows:

Pialoux *et al.* and Egan *et al.* do not disclose SEQ ID NO:64. Walker *et al.* explicitly suggests HIV-1 epitope in the reverse transcriptase of the amino acid sequence, NPDIVIYQYMDDLYVGSDLEIGQHR (peptide 50) to specifically stimulate CD8+ T cell immune response. See page 9517, left column, Table 4, line 12.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the epitope of Pialoux *et al.* and Egan *et al.* to the epitope comprising an amino acid sequence of SEQ ID NO:64. One having ordinary skill in the art would have been motivated to do this because the peptide 50 has been clearly defined as a potent CTL epitope from the most highly conserved region of HIV genome, as per suggested by Walker *et al.*, who established a reasonable expectation of success by describing that this epitope induces specific cytotoxicity in target cells. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argue that Walker *et al.* do not teach or suggest that the disclosed CTL epitopes should be featured in a prime-boost method for generating a CD8+ T cell immune response in a mammal against a target antigen like HIV, nor do Walker *et al.* disclose or suggest administering to a mammal a boosting composition comprising a non-replicating or replication-impaired recombinant virus vector.

Applicants' arguments have been fully considered but are not persuasive because the limitations not disclosed in Walker *et al.* have already been described in Pialoux *et al.* and Egan *et al.* as set forth above. The instant rejection is based on the invention as a whole rather than Walker *et al.* alone. In response to applicant's arguments

against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

New Claim Rejections - 35 USC § 103

Claims 1-4, 6, 7, 10, 12, 14-16, 27, 28, 32 and 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Li *et al.* (1993, reference No. AU4 in IDS filed on 06 July 2004) in view of Sutter *et al.* (1992, reference No. C52 in IDS filed on 09 November 2006) and Stoute *et al.* (1997, January).

Li *et al.* describe priming with recombinant influenza virus followed by boosting with recombinant vaccinia virus induces CD8+ T-cell-mediated protective immunity against malaria. The sequence of immunization appears to be crucial, since a primer injection with recombinant vaccinia virus, followed by a booster injection with recombinant influenza virus, failed to induce protection. The protection induced by immunization with these recombinant viruses is mostly mediated by CD8+ T cells. See abstract. Suggested routes of administration were i.p., by aerosol, and intravenous injection. See p. 5215, left column.

Li *et al.* do not describe a replication-impaired or non-replicating recombinant virus vector in the boosting composition and an adjuvant.

Sutter *et al.* describe a non-replicating vaccinia vector, modified vaccinia Ankara (MVA) strain that has been safety tested in humans. See Abstract.

Stoute *et al.* describe malaria vaccine formulations in three kinds of adjuvants: alum and monophosphoryl lipid A (SBAS4), an oil-in-water emulsion (SBAS3), and an oil-in-water emulsion plus the immune stimulants monophosphoryl lipid A and QS21 (SBAS2). The vaccines were administered intramuscularly. See p. 87, Study Design and Vaccines. Stoute *et al.* further describe that SBAS2 is the most efficacious adjuvant. See p. 90, Discussion.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the priming and boosting compositions of Li *et al.* so as to replace the vaccinia vector with a safer non-replicating MVA vector as taught by Sutter *et al.* One having ordinary skill in the art would have been motivated to do this because a live vaccinia virus is infectious while MVA does not replicate in mammalian cells yet expresses recombinant genes efficiently, as suggested by Sutter *et al.*

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the priming and boosting compositions of Li *et al.* so as to further comprise the SBAS2 adjuvant as taught by Stoute *et al.* One having ordinary skill in the art would have been motivated to do this because SBAS2 may also provide signals required to up-regulate co-stimulatory molecules on antigen-presenting cells, induce expression of molecules that permit these cells to travel to target tissues, or induce production of cytokines that mediate protection, as per suggested by Stoute *et al.* There would have been a reasonable expectation of success, given the results that the SBAS2 formulation proved superior for inducing strong antibody responses and strong antigen-specific delayed hypersensitivity in primates and proliferative and

cytolytic T cell responses in mice, as taught by Stoute *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim Objections

Claim 31 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 31 recites a group of CD8+ T cell epitopes against other pathogens than malaria and hence fails to further limit base claim 27.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
26 March 2007

Louise Humphrey, Ph.D.
Assistant Examiner

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